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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 01/27/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n No.

09/698,341

Applicant(s)

SORGE ET AL.

Examiner

Richard G Hutson

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-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 07 November 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5-10,12-47 and 85-88 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) 1 and 5 is/are allowed.
- 6) ☐ Claim(s) 2,3,6-10,12-47 and 85-88 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10/27/2000 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Applicants amendment of claims 6, 10 and 88 is acknowledged. Claims 1-3, 5-10, 12-47 and 85-88 are at issue and present for examination. Applicants' arguments filed on 11/7/2002, Paper No. 20, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claim 32 is objected to because of the following informalities: Claim 32 recites the amino acid "asparagene". This should be "asparagine".

Appropriate correction is required.

Drawings

The drawings are objected to for the reasons stated on the attached form PTO-948. Note, applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Specification

The disclosure is objected to because of the following informalities: Figures 14 and 15 each comprise a number of sequences but there is no indication in the figure or

the description of the figure as to the associated SEQ ID NOs. As per MPEP Section **2422.02**, *The Requirement for Exclusive Conformance; Sequences Presented in Drawing Figures*, it should be noted, though, that when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings.

On page 16, line 18 applicants recite the amino acid "asparagene". This should be "asparagine".

On page 7, line 8, applicants recite "These organisms grow at temperatures higher than **901C...**" It is believed this is a typographical error which should be corrected.

On page 8, line 19, applicants recite "Dong et al. 1993, J. Biol. Chem. 268, **26143**". This should be "Dong et al. 1993, J. Biol. Chem. 268, **24163**"

Appropriate correction is required.

Applicants continue to argue the previous objection to the specification that the recitation on page 23, line 5, "...the conventional deoxynucleotides dATP, dCTP, dGTP and TTP...", is unclear in its reference to TTP as being included as a deoxynucleotide. Applicants arguments presented in previous papers, as well as the present after-final response are NOT persuasive, as the examiner continues to believe that "dTTP" is the proper abbreviation for deoxythymidine triphosphate, and not "dideoxythymidine

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triphosphate" as asserted by applicants, and "TTP" is a proper abbreviation for thymidine triphosphate. However, in light of applicants continued insistence that "the abbreviation TTP refers to the conventional, deoxy-form of the thymidine 5'-triphosphate, the objection is withdrawn and applicants recitation of "TTP" is interpreted in this application based on applicants arguments as standing for the "deoxy-form of the thymidine 5'-triphosphate" .

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2 and 88 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The rejection is stated in the previous office action, Paper No. 9, 8/15/2001, traversed in Paper No. 16, 10/9/2002 and maintained in the previous office action, Paper No. 12, 5/7/2002, as it applied to previous claims 6-15.

Applicants have amended claims 6, 10 and 88. Claim 88 is currently drawn to an isolated recombinant Family B DNA polymerase from *Thermococcus* species JDF-3 that comprises an alanine to threonine mutation at a site corresponding to A 485 of SEQ ID NO: 2. Applicants continue to traverse the rejection of the instant claims under 35

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U.S.C. 112, first paragraph, on the basis that the application consistently refers to the claimed Family B DNA polymerase from *Thermococcus* species JDF-3 with respect to SEQ ID NO: 2 and this therefore provides a literal boundary for what is meant by "Family B DNA polymerase from *Thermococcus* species JDF-3. Applicants further submit that claim 6 and its dependent are expressly limited to "an isolated Family B DNA polymerase from *Thermococcus* species JDF-3 and that the only Family B DNA polymerase from *Thermococcus* species JDF-3 reported in the specification is that of SEQ ID NO: 2 and mutants with amino acid substitutions stated relative to SEQ ID NO: 2, thus it is clear that the term "Family B DNA polymerase from *Thermococcus* species JDF-3" is used with respect to a polymerase of SEQ ID NO: 2 or a mutant thereof. Applicants finally submit that because the Family B DNA polymerase from *Thermococcus* species JDF-3 is consistently referred to with respect to SEQ ID NO: 2, one of skill in the art need only have available SEQ ID NO: 2 in order to generate Family B DNA polymerases from *Thermococcus* species JDF-3 that fall within the class.

While it is admitted that applicants do teach the *Thermococcus* strain JDF-3 polynucleotide and amino acid sequences in the specification and teach some substitutions which are encompassed by the currently rejected claims, the claims do not recite any specific polynucleotide or amino acid sequences and thus claims to a Family B DNA polymerase from *Thermococcus* species JDF-3 require the *Thermococcus* species JDF-3. While the claims are read in light of the specification, the specification is not limiting to the claims. If it is applicants intent that the claimed *Thermococcus* strain JDF-3 Family B DNA polymerase has a specific sequence corresponding to a specific

SEQ ID NO:, then it is suggested that applicants amend the specification to include such a limitation, otherwise, the organism from which the polymerase is isolated, must be fully disclosed or shown to be publicly known and freely available. Accordingly, it is deemed that a deposit of this strain should have been made in accordance with 37 CFR 1.801-1.809.

Applicants argument is not found persuasive and if it is applicants intent that "Family B DNA polymerase from *Thermococcus* species JDF-3" is equivalent to that DNA polymerase having the amino acid sequence of SEQ ID NO: 2, then it is suggested that applicants amend each of the rejected claims as such.

Claims 6-10, 12-47 and 85-87 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is stated in the previous office action, as it applied to claims 6-45, Paper No. 9, 8/15/2001, traversed in Paper No. 16, 10/9/2002 and maintained in the previous office action, Paper No. 12, 5/7/2002.

Applicants have amended claims 6 and 10 and continue to traverse the rejection under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention on the basis that applicants have provided a number of different

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individual mutants and a description of the structure/function relationship between "the conserved structural motifs" and Exo activity and particular amino acid changes.

Applicants submit that with respect to 3' to 5' exonuclease deficiency as recited in claim 6, applicants specification describes six different individual mutants of

Thermococcus species JDF-3 Family B DNA polymerase that target a region correlated with 3' to 5' Exo activity in related polymerases, specifically D141A, D141N, D141S, D141T, D141E and E143A as well as the double mutant D141A + E143A and that three of the single mutants and the double mutant exhibited dramatically reduced 3' to 5' Exo activity, representing a reduction to practice through four working examples of different mutants that fall within the claim requiring 3' to 5' exonuclease deficiency.

Applicants further submit that in addition to the working examples, applicants specification provides a correlation between structure and function with regard to the 3' to 5' activity in its reference to the replacement of conserved aspartic or glutamic acid residues with alanine in Vent and Pfu polymerases, as well as conservative substitutions of 9°N-7 DNA polymerase.

This argument is not found persuasive, because as previously pointed out the disclosed species are not representative of the infinite number of species within the claimed genus and the structure/function relationship discussed does not provide adequate guidance that helps in the description of the claimed genus that is drawn to **any** isolated recombinant mutant of the DNA polymerase of SEQ ID NO: 2 that is 3' to 5' exonuclease deficient. The claimed genus comprises mutations of not only those described by applicants specification (i.e. D141, E143 of SEQ ID NO: 2), but any of the

potentially infinite number of mutations comprising any and all substitutions, modifications, deletions and insertions of any number of amino acids of SEQ ID NO: 2.

With regard to newly amended claim 10, applicants submit that the claim satisfies the written description requirement because the claim requires that the isolated Family B DNA polymerase having reduced discrimination against non-conventional nucleotides "has a mutation in the Region II consensus sequence DXXSLYPSII." Applicants submit that the specification provides 12 mutants (at two positions, L408 and P410) as well as a number of double mutants, which have a reduced discrimination against non-conventional nucleotides and that applicants describe other Family B DNA polymerases mutated in the Region II consensus and the effects of these mutations on discrimination. This argument is not persuasive because while applicants submission may adequately describe those mutants of SEQ ID NO: 2, having a mutation in the Region II consensus sequence DXXSLYPSII, applicants have not adequately described any Family B DNA polymerase having a mutation in the Region II consensus sequence DXXSLYPSII nor have applicants given any guidance as to the occurrence of this consensus sequence in other Family B DNA polymerases. Further as this is a consensus sequence how does one determine the same region in these other Family B DNA polymerases, and would not any derivation from the consensus sequence not be considered to a mutation in the Region II consensus sequence DXXSLYPSII?

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 85 recites the limitation "said mutation in Region II" in the DNA polymerase of claim 10. There is insufficient antecedent basis for this limitation in the claim. It is suggested that claim 85 be amended such as "said mutation in Region II consensus sequence"

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6, 10, 14, 15 and 87 are rejected under 35 U.S.C. 102(a) as being anticipated by Gardner et al. (Nucleic Acids Research Vol 27, No. 12, pages 2545-2553, 1999, See IDS ref C).

Gardner et al. teach the determinants of nucleotide sugar recognition in an archaeon DNA polymerase, specifically the Family B DNA polymerase, Vent DNA polymerase. Gardner et al. specifically teach a Y412V variant that incorporates

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ribonucleotides at least 200 fold more efficiently than the wild-type enzyme. Thus claims 6, 10, 14, 15 and 87 are anticipated by Gardner et al. Claim 6 is included in this rejection because as applicants have not taught when a mutant of a specific DNA polymerase (i.e. JDF-3 Family B DNA polymerase) becomes a mutant of a different DNA polymerase (i.e. human DNA polymerase α), the claim is interpreted as any DNA polymerase that is not the same as the recited wildtype DNA polymerase is considered a mutant.

Claims 6, 10, 14, 15 and 87 are rejected under 35 U.S.C. 102(b) as being anticipated by Dong et al. (Journal of Biological Chemistry, Vol 268, No. 15, pages 24163-24174, 1993).

Dong et al. teach a mutant of the Family B DNA polymerase, human DNA polymerase α , comprising Y865S and Y865F. This mutant is 3' to 5' exonuclease deficient, and has a reduced discrimination against non-conventional nucleotides. Thus claims 6, 10, 14, 15 and 87 are anticipated by Dong et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned

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are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

A handwritten signature in black ink, appearing to read 'Richard Hutson', with a long horizontal line extending to the right.

Richard Hutson Ph.D.
Patent Examiner
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January 24, 2003